

Impact of short-acting vs. long-acting antipsychotic use on time in seclusion on a forensic assessment unit: a retrospective chart review

Sumani Vij BSc PharmD

St. Joseph's Health Care London Year 1 Pharmacy Residency

Research Project Manuscript

(2023-2024)

Acknowledgements

Thank you to the Residency Project Team and Pharmacy Residency Advisory Committee for your support on this project.

Residency Project Team

Brandon LeBlanc BSc PharmD^{1,2}

Nicholas Woods MSc MScFN R.D³

Jason Quinn MD FRCPC^{1,4}

2023 – 2024 Pharmacy Residency Advisory Committee

Denise Kreuzwiser

Andrey Andriets

Victor Tsang

Ayesha O’Hara

Rachel Lee

Bruce Li Shing Pun

Tajana Jokic

Ashley Elsie

Geoff Bellingham

Feng Chang

¹Department of Psychiatry, Schulich School of Medicine & Dentistry, Western University, London, Canada ²Department of Pharmacy, St. Joseph’s Health Care London, Canada ³Faculty of Health Sciences, Western University, London, Canada, ⁴Southwest Centre for Forensic Mental Health Care, St. Joseph’s Health Care London, Canada,

Table of Contents

ABSTRACT	4
LIST OF ABBREVIATIONS	5
INTRODUCTION	6
METHODS	7
RESULTS	9
DISCUSSION	11
CONCLUSION	13
REFERENCES	15
APPENDIX 1	17
ENROLLMENT CRITERIA	17
APPENDIX 2A	18
ANTIPSYCHOTIC AGENTS	18
APPENDIX 2B	19
MOOD STABILIZER AGENTS	19
APPENDIX 2C	20
ANXIOLYTIC AGENTS	20
APPENDIX 3	21
LAWSON HEALTH RESEARCH INSTITUTE FINAL APPROVAL NOTICE	21
TABLES	22
TABLE 1. BASELINE CHARACTERISTICS	22
TABLE 2. CHARACTERISTICS OF INDEX ANTIPSYCHOTICS PRESCRIBED	23
TABLE 3. MULTIVARIABLE REGRESSION ANALYSIS – PRIMARY OUTCOMES	24
TABLE 4. MULTIVARIABLE LINEAR REGRESSION – SECONDARY OUTCOMES	25
FIGURES	26
FIGURE 1. STUDY ENROLLMENT	26
FIGURE 2. BOX AND WHISKER PLOT FOR TIME IN SECLUSION FOR LA AND SA ANTIPSYCHOTIC COHORTS	27
FIGURE 3. ANTIPSYCHOTIC ADMINISTRATION IN LAST 24 HOURS OF SECLUSION	28

Abstract

Background: Seclusion, a strategy used to manage aggressive behavior in patients posing safety risks, can result in prolonged hospitalization and trauma. Antipsychotics, used to treat major mental illnesses including schizophrenia and bipolar disorder, are available as long-acting (LA) and short-acting (SA) formulations, with evidence suggesting LA antipsychotics may improve patient outcomes such as reducing hospitalizations and decreasing aggression, which is primarily driven by an increase in medication adherence.

Objective & Methods: This retrospective chart review evaluated the impact of SA versus LA antipsychotics on seclusion duration in adult patients at the Southwest Centre for Forensic Mental Health Care (Ontario, Canada) between April 1, 2017, and December 31, 2023.

Results: Of 83 patients (60 in the SA cohort, 23 in the LA cohort), no significant difference was found in seclusion time for SA compared to LA antipsychotics (2.7 hours, 95% CI: -67.8, 62.5, $p > 0.05$). Mood stabilizer use was associated with longer seclusion (SA: 112.7 hours, LA: 215.3 hours, $p < 0.05$), but no difference was observed with anxiolytics.

Conclusion: Clinicians should consider individual patient needs and treatment contexts when prescribing antipsychotics. Further research is warranted to investigate broader patient outcomes and the implications of antipsychotic formulations in forensic mental health.

List of Abbreviations

LA	long-acting
SA	short-acting
SWC	Southwest Centre
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5th edition
EMR	Electronic Medical Records
AHFS	American Hospital Formulary System

Introduction

Seclusion is a common intervention employed by psychiatric units, including forensic mental health settings, whereby patients exhibiting aggressive behavior who pose a safety risk to themselves and others are placed in isolation.¹ However, the impact of seclusion on patients can be detrimental, leading to prolonged hospitalization, decreased quality of life, and reported experiences of trauma.¹ Additionally, seclusion may require the involvement of multiple clinical staff and the administration of medications, often in combination with restraints. Several studies suggest that seclusion not only negatively impacts patients but can also strain the therapeutic relationship between patients and healthcare providers.^{2,3} Clinical staff members report experiencing stress, emotional exhaustion and moral conflict when enforcing seclusion.^{2,3} Furthermore, time spent enacting seclusion procedures may contribute to staff burnout and can consume valuable clinical resources. There is ongoing debate around the necessity of seclusion, with some advocating for its complete discontinuation while acknowledging its ongoing prevalence.³⁻⁵ Institutions such as Pennsylvania State Hospitals that have successfully reduced use of seclusion have shown improved patient outcomes such as decreased reliance on “as needed” or immediate medication orders, and fewer injuries to both patients and staff.⁵⁻⁶ Thus, finding ways to reduce seclusion time remains a worthwhile goal in psychiatric settings.

Antipsychotics, a cornerstone in the treatment of major mental health conditions like schizophrenia and bipolar disorder, are available in various formulations including short-acting (SA) oral formats and injections, as well as long-acting (LA) injectable options. LA antipsychotics, such as paliperidone and aripiprazole, have gained popularity due to their extended duration of action reduced frequency of administration, compared to SA medications.⁷ While LA antipsychotics typically incur higher acquisition costs, they have been shown to improve medication compliance rates and reduce relapses to offset initial expenses. For instance, studies show that LA antipsychotics reduce length of hospital stay and number of emergency department visits, contributing to annual cost savings from fewer inpatient resources despite their higher cost.⁷⁻⁹ While research comparing oral SA to LA injectable antipsychotics show mixed results,¹⁰⁻¹² a 2021 systematic review by Kishimoto et al. demonstrated that LA antipsychotics, compared to SA oral antipsychotics, are associated with fewer relapses, which may be attributable to their longer duration of action and lower administration frequency.¹³ Of note, a randomized control trial by Arango et al. showed how switching to a LA antipsychotic reduced aggression and violent behavior through improved medication compliance.¹²

Given the detrimental effects of seclusion and the potential benefits of LA antipsychotics, we sought to investigate whether the use of LA antipsychotics could reduce time spent in seclusion, thereby improving overall patient outcomes. While there is limited data examining seclusion as a direct outcome of antipsychotic treatment, a retrospective study from the Netherlands suggests that antipsychotics may delay the time to seclusion for hospitalized patients.¹⁴ The study found that individuals treated with antipsychotics had a median time to seclusion from admission of 7 days, as opposed to 2.5 days for those not treated.¹⁴ This study indicates a potential relationship between antipsychotic use and seclusion outcomes.

In Canada, accused persons facing criminal charges may be found “Unfit to Stand Trial Due to Mental Disorder” if their mental disorder renders them unable to understand the nature and object of their proceedings, the possible consequences of their proceedings, or their ability to communicate with counsel.¹⁵ Courts may then choose to order mandatory treatment pursuant to a Treatment Order to render them fit to stand trial within a period not exceeding 60 days. Typically, patients with treatable psychotic conditions, such as schizophrenia or bipolar and related conditions, are ordered to receive treatment with medications, including oral or injectable antipsychotics in inpatient forensic psychiatric settings.

Our study aims to contribute to the existing literature on clinical outcomes associated with SA versus LA antipsychotics. We hypothesize that at our forensic mental health site, the use of LA antipsychotics will reduce time spent in seclusion for those with a treatment order by allowing for quicker stabilization of symptoms.

Methods

Study Design

This retrospective observational cohort study examined adult patients admitted to Southwest Centre (SWC) for Forensic Mental Health Care (St. Thomas, Ontario, Canada) who were placed in seclusion on a treatment order between April 1, 2017, and December 31, 2023. To be included in the analysis, individuals must have been administered either SA or LA antipsychotics within 7 days of their seclusion order.

The primary objective of this study was to investigate whether there is a difference in time spent in seclusion between patients treated with SA versus LA antipsychotics. Secondary outcomes of this study included determining whether time spent in seclusion varied between patients taking mood stabilizers or anxiolytics and those not taking them within each group.

Patient Population

This study only included individuals placed in seclusion under treatment orders which ensured exposure to antipsychotic therapy. Those admitted to SWC for other reasons such as forensic assessments were not included as no changes to treatment is made for these patients.

Inclusion criteria required that patients had diagnostic impressions of schizophrenia and other psychotic disorders, or bipolar and related disorders, as defined by the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) as antipsychotics are the mainstay treatment for these conditions. For patients who underwent seclusion more than once while admitted to SWC with a treatment order, only the first seclusion episode within the designated study timeframe was analyzed to minimize confounders related to antipsychotic treatment resistance.

Individuals prescribed clozapine, a SA antipsychotic, were excluded as it is not typically prescribed in a treatment order due to time constraints and the complexity of prescribing and monitoring clozapine. Refer to *Appendix 1* for complete list of enrollment criteria.

Drug Classification

The specific agents in each drug class investigated in this study (i.e. SA antipsychotics, LA antipsychotics, mood stabilizers, and anxiolytics) were classified according to the American Hospital Formulary System (AHFS), a pharmacological-therapeutic classification system widely used across North America for formulary classification.¹⁶ The list was further refined through collaboration with forensic psychiatrists at SWC, taking into account their expertise and cross-referencing with the agents available on the Canadian market. See *Appendices 2a-2c* for a full list of drug agents used in this study.

For the purposes of this study SA antipsychotics were defined as any formulations of antipsychotics which require daily or more than once daily dosing. As such, short-acting intramuscular antipsychotics were also included in this category. LA antipsychotics were defined as formulations with extended durations of action, typically lasting several weeks to months.

Study Process

This study was approved by The Office of Research Ethics at Western University and Lawson Health Research Institute (*R-24-112, Appendix 3*). A comprehensive list of adults admitted to SWC who were placed in seclusion during the study period

was generated. Electronic medical records (EMR) were then reviewed to determine eligibility based on the inclusion/exclusion criteria. Eligible patients were stratified into either the SA or LA antipsychotic group based on the initial antipsychotic administered during the seclusion period. For the purposes of this study, this initial antipsychotic is referred to as the “index antipsychotic”.

Defining Seclusion Duration

Time spent in seclusion was measured in hours. If a patient was temporarily removed from seclusion but subsequently returned within 24 hours, the entire duration was counted as a single seclusion episode, reflecting the failure to transition out of seclusion. This is because some patients may be trialed out of seclusion into enhanced observation following assessment from the psychiatrist but may return to seclusion due to agitation/aggressive behavior. Seclusion orders within the EMR typically include an expiry date, usually 24 hours after initiation, as well as a completion date, though discrepancies between these dates may arise. To address such discrepancies, progress notes from the seclusion period were used to accurately determine the time of release. If the release time documented in progress notes differed from both the expiry and completion times, then the date and time of the signed note were used as the definitive end of seclusion.

Statistical Analysis

Descriptive statistics were used in this study to better understand demographic and clinical characteristics of the patient population. A multivariable linear regression analysis was conducted to assess differences in the number of hours spent in seclusion between patients in the SA antipsychotic group and those in the LA antipsychotic group.

Results

As shown in *Figure 1*, a total of 205 patient charts were screened, and 83 patients met the eligibility criteria. The most common reason for exclusion was that patients were not placed in seclusion on a treatment order. Of the 83 eligible patients, 60 individuals were placed in the SA cohort and 23 in the LA cohort.

Baseline characteristics were comparable between the two cohorts. As shown in *Table 1*, age and sex at birth were similar in both groups. Over 90% of the patients in each cohort were diagnosed with schizophrenia or other related psychotic disorders. The median time in seclusion was 66.2 hours (IQR: 24.4 – 111.2) for the SA cohort and 37.3 hours (IQR: 23.2 –

97.7) for the LA cohort. However, as depicted in *Figure 2*, there was significant variability in the length of time spent in seclusion ranging from 2.75 to 722.9 hours, with considerable outliers observed in both cohorts.

Antipsychotic Prescribing Patterns

Table 2 details the index antipsychotic prescribing patterns. In the SA cohort, oral olanzapine was the most prescribed SA antipsychotic, administered 12 times with an average dose of 12.9 mg. Zuclopenthixol acetate was the most common SA intramuscular antipsychotic, given 14 times at an average dose of 87.5 mg. In the LA cohort, paliperidone long-acting injection (LAI) was most frequently prescribed, administered 11 times at an average dose of 127.8 mg.

On average, patients were prescribed more than one concomitant antipsychotic (SA: 1.5 (SD \pm 1.3), LA: 1.8 (SD \pm 1.6)).

Additionally, 29% of individuals were administered mood stabilizers, while 82% were administered anxiolytics; this indicates most patients were on complex medication regimens for treatment and stabilization.

Figure 3 depicts the antipsychotics administered in the last 24 hours for both cohorts. By the end of the seclusion episodes, considerable overlap was observed between the index antipsychotic cohort and other prescribed formulations. In the SA cohort, there were 27 instances where patients received LA injection at some point during seclusion. Similarly, in the LA cohort, there were 20 instances where oral SA antipsychotics were administered on the last day of seclusion and 4 instances where intramuscular SA antipsychotics were administered.

Multivariable Regression Analysis

Multivariable linear regression analysis revealed that when age, sex, and diagnosis constant, no significant difference was found in hours of seclusion among those prescribed SA compared to LA antipsychotics (2.7 hours, 95% CI: -67.8, 62.5, $p > 0.05$) (*Tables 3 and 4*). Patients prescribed mood stabilizers, however, spent significantly more time in seclusion within both cohorts (SA: 112.7 hours, LA: 215.3 hours, $p < 0.05$) compared to those not on mood stabilizers. No significant difference in seclusion time was observed for those prescribed anxiolytics within either cohort (SA: 25.3 hours, LA: 25.5 hours, $p > 0.05$) compared to those not on anxiolytics.

Discussion

Primary Outcomes

Our study found no significant difference in seclusion duration between patients receiving SA versus LA antipsychotics. This finding contradicts our initial hypothesis that LA antipsychotics, due to their longer duration of action, would lead to faster stabilization and subsequently less seclusion time. One explanation for this is that LA antipsychotics are typically associated with better adherence but this was not a focus because compliance is mandated in our population due to the treatment orders. In a non-treatment order setting, patients refusing oral medications would typically have their therapy switched to injectable formulations to better support adherence. When adherence is mandated, the benefit of LA antipsychotics to improve adherence may be less relevant.

Factors such as dosage, individual patient response to medication, and the overall complexity of treatment regimens (e.g., the frequent use of multiple antipsychotics in both cohorts) may have influenced our findings. Given that seclusion is used for the acute management of agitation and aggression, it is possible the prescribed medications were not administered for a sufficient duration to provide stabilization, instead only managing immediate symptoms. This is supported by Stolker et al. Who showed that antipsychotic prescribing, as a class, can delay time to seclusion.¹⁴ The considerable variability in seclusion times observed in our study (2.8 – 722.9 hours) highlights the challenge of using seclusion duration as a measure for the efficacy of LA antipsychotics.

Moreover, significant overlap existed between the SA and LA groups, with patients often receiving multiple antipsychotics during their seclusion episode. On 27 occasions an index SA antipsychotic patient was later administered LA antipsychotics during seclusion likely due to a change in therapy, adjunctive therapy, or as part of an initiation regimen for LA antipsychotics. This overlap makes it difficult to draw clear conclusions about the isolated effects of either antipsychotic formulation.

Secondary Outcomes

Regardless of whether they were in the SA or LA cohort, patients prescribed mood stabilizers spent significantly more time in seclusion compared to those not taking these medications. This finding may be confounded by the severity of the underlying condition, as mood stabilizers are typically prescribed for patients with more severe psychiatric symptoms.

Mood stabilizers are used to treat patients presenting with elements of emotional dysregulation or a history of requiring mood stabilizers for stabilization based on their medical records. In patients diagnosed with schizophrenia and other psychotic disorders, which accounted for more than 90% of our sample population, mood stabilizers are used as an adjunct to antipsychotics for patients not responding adequately to first line treatments. These patients often require longer periods of stabilization, which could explain the extended seclusion times.

No significant difference in seclusion time was found for patients prescribed anxiolytics compared to those not prescribed anxiolytics. This is likely due to the large proportion of patients in both cohorts being prescribed these medications (SA: 78.3%, LA: 91.3%).

Clinical Implications

The lack of a significant difference in seclusion time between patients treated with SA versus LA antipsychotics suggests that both formulations evoke similar outcomes when managing psychiatric symptoms during seclusion. While LA antipsychotics are often favored in clinical settings for their ability to maintain stable plasma concentrations and improve adherence in the long term, our findings indicate they may not confer additional benefits over SA antipsychotics in the context of seclusion duration. This suggests that in situations where adherence is enforced, such as inpatient forensic settings, SA antipsychotics can exhibit similar treatment outcomes as LA formulations. Clinicians should carefully evaluate the choice between SA and LA antipsychotics based on individual patient profile, while also considering factors such as the drug's pharmacokinetics, side effect profiles, and the patient's clinical condition and disposition, to ensure optimal treatment outcomes.

SA antipsychotics offer certain advantages, such as more flexible dosing schedules and easier dose titration. In situations where patients experience side effects or lack of response to treatment, SA antipsychotics can be discontinued faster and avoid the sustained high plasma levels associated with LA formulations as well as associated polypharmacy. SA antipsychotics generally have lower drug acquisition costs, which may be beneficial for inpatient settings where adherence is enforced through treatment orders. The frequent dosing required for SA antipsychotics can, however, lead to more patient-staff interactions during seclusion; if the use of restraints is increased during these interactions potentially worsen outcomes may ensue.

While adherence is not a significant issue in the studied population, LA antipsychotics may be more beneficial for patients transitioning to community or outpatient settings, where adherence may be less consistent.

Limitations

Several limitations must be considered when interpreting these findings. First, the sample size, particularly in the LA cohort, was relatively small, which may limit the generalizability of the results. Additionally, while we controlled for age, sex, and diagnosis in the multivariable regression model, other potential confounders such as the severity of psychosis, dose of the antipsychotic, and staff-related factors were not accounted for. The variability in length of seclusion time also suggests that individual patient factors played a substantial role in the outcomes. Given limited access to previous records and missing histories, our team was not able to obtain data on the severity of illness including number of relapses, hospitalizations, seclusion history outside SWC, or antipsychotic agents trialed in the past. As such, the retrospective design and lack of access to prior seclusion history or data on the severity of illness made it difficult to fully understand the impact of previous treatment decisions.

This study focused on the duration of seclusion as a primary outcome, but did not assess other important measures such as symptom improvement or patient quality of life, which could provide a more comprehensive understanding of the impact of antipsychotic treatment formulations.

Conclusion

This study demonstrates similar outcomes for both SA and LA antipsychotics in managing acute psychiatric symptoms during seclusion, with no significant difference in seclusion duration between the two formulations. This challenges our initial hypothesis that LA antipsychotics would offer better stabilization and result in shorter seclusion times. Treatment decisions should therefore be guided by individual patient needs and clinical context rather than antipsychotic formulation. SA antipsychotics offer greater flexibility in dosing and cost-effectiveness for inpatient settings where adherence is enforced. LA antipsychotics can reduce staff exposure to agitated patients and may be beneficial for cultivating long-term adherence for patients with schizophrenia transitioning to outpatient care.

Future studies should explore not only broader clinical outcomes such as symptom improvement and quality of life but also consider the number of seclusion episodes as a more comprehensive measure of stabilization. Examining multiple seclusion

episodes may provide better insight into the efficacy of antipsychotic formulations in maintaining symptom control over time. Further research, preferably with a prospective design, is needed to determine the full impact of antipsychotic formulations on patient outcomes in forensic mental health populations.

References

1. Chieze M, Hurst S, Kaiser S, Sentissi O. Effects of Seclusion and Restraint in Adult Psychiatry: A Systematic Review. *Front Psychiatry*. 2019;10:491. Published 2019 Jul 16. doi:10.3389/fpsy.2019.00491
2. Kinner SA, Harvey C, Hamilton B, et al. Attitudes towards seclusion and restraint in mental health settings: findings from a large, community-based survey of consumers, carers and mental health professionals. *Epidemiol Psychiatr Sci*. 2017;26(5):535-544. doi:10.1017/S2045796016000585
3. Yurtbasi MK, Melvin G, Pavlou C, Gordon M. Staff perspectives on the effects of seclusion in adolescent psychiatric inpatient care. *Int J Ment Health Nurs*. 2023;32(2):567-578. doi:10.1111/inm.13102
4. LeBel JL, Duxbury JA, Putkonen A, Sprague T, Rae C, Sharpe J. Multinational experiences in reducing and preventing the use of restraint and seclusion. *J Psychosoc Nurs Ment Health Serv*. 2014;52(11):22-29. doi:10.3928/02793695-20140915-01
5. Smith GM, Altenor A, Altenor RJ, et al. Effects of Ending the Use of Seclusion and Mechanical Restraint in the Pennsylvania State Hospital System, 2011-2020. *Psychiatr Serv*. 2023;74(2):173-181. doi:10.1176/appi.ps.202200004
6. Smith GM, Ashbridge DM, Davis RH, Steinmetz W. Correlation between reduction of seclusion and restraint and assaults by patients in Pennsylvania's state hospitals. *Psychiatr Serv*. 2015;66(3):303-309. doi:10.1176/appi.ps.201400185
7. Hodgson RE. Evaluating the cost and clinical effectiveness of long-acting, injectable aripiprazole and paliperidone palmitate once a month in a real-world setting [published correction appears in *Clinicoecon Outcomes Res*. 2019 Sep 09;11:dlxvii. doi: 10.2147/CEOR.S228414]. *Clinicoecon Outcomes Res*. 2019;11:517-524. Published 2019 Aug 13. doi:10.2147/CEOR.S191198
8. Lachaine J, Lapierre ME, Abdalla N, Rouleau A, Stip E. Impact of switching to long-acting injectable antipsychotics on health services use in the treatment of schizophrenia. *Can J Psychiatry*. 2015;60(3 Suppl 2):S40-S47.
9. Stip E, Lachaine J. Real-world effectiveness of long-acting antipsychotic treatments in a nationwide cohort of 3957 patients with schizophrenia, schizoaffective disorder and other diagnoses in Quebec [published correction appears in *Ther Adv Psychopharmacol*. 2018 Sep 03;8(11):327. doi: 10.1177/2045125318799889]. *Ther Adv Psychopharmacol*. 2018;8(11):287-301. Published 2018 Jun 22. doi:10.1177/2045125318782694
10. Wang D, Schneider-Thoma J, Sifis S, et al. Efficacy, acceptability and side-effects of oral versus long-acting-injectables antipsychotics: Systematic review and network meta-analysis. *Eur Neuropsychopharmacol*. 2024;83:11-18. doi:10.1016/j.euroneuro.2024.03.003
11. Weiden PJ, Schooler NR, Weedon JC, Elmouchtari A, Sunakawa A, Goldfinger SM. A randomized controlled trial of long-acting injectable risperidone vs continuation on oral atypical antipsychotics for first-episode schizophrenia patients: initial adherence outcome. *J Clin Psychiatry*. 2009;70(10):1397-1406. doi:10.4088/JCP.09m05284yel
12. Arango C, Bombín I, González-Salvador T, García-Cabeza I, Bobes J. Randomised clinical trial comparing oral versus depot formulations of zuclopenthixol in patients with schizophrenia and previous violence. *Eur Psychiatry*. 2006;21(1):34-40. doi:10.1016/j.eurpsy.2005.07.006

13. Kishimoto T, Hagi K, Kurokawa S, Kane JM, Correll CU. Long-acting injectable versus oral antipsychotics for the maintenance treatment of schizophrenia: a systematic review and comparative meta-analysis of randomised, cohort, and pre-post studies. *Lancet Psychiatry*. 2021;8(5):387-404. doi:10.1016/S2215-0366(21)00039-0
14. Stolker JJ, Hugenholtz GWK, Heerdink ER, Nijman HLI, Leufkens HGM, Nolen WA. Seclusion and the use of antipsychotics in hospitalized psychiatric patients. *Psychol Crime Law*. 2005;11(4):489-495. doi:10.1080/10683160500256743
15. Criminal Code, RSC 1985, c C-46, s 672.58. <https://laws-lois.justice.gc.ca/eng/acts/c-46/page-109.html>. Accessed October 27, 2024.
16. AHFS classification - drug assignments. AHFS Drug Information. January 10, 2023. Accessed October 28, 2024. <https://ahfsdruginformation.com/ahfs-classification-drug-assignments/>.

Appendix 1

Enrollment Criteria

Inclusion Criteria

Is the patient 18 years-of-age or older?	Yes	No
Was the patient placed in seclusion on a treatment order?	Yes	No
Was the patient exposed to either short-acting or long-acting antipsychotic within 7 days of seclusion initiation or until seclusion period ends, whichever is shorter? <i>(Note: patient is eligible if they received long-acting antipsychotic prior to seclusion as the duration of action overlaps with the seclusion period)</i>	Yes	No
Does the patient have a working diagnosis/diagnostic impression of either (as defined in the DSM-5): iii. Schizophrenia and other psychotic disorder iv. Bipolar and related disorders	Yes	No
Is this the patient's first seclusion while admitted to Southwest Center (SWC) either in this visit, or a previous visit? <i>(Note: Only the initial seclusion event is being investigated in this study. As such, if selecting "no" to this eligibility screening question, the co-investigator collecting the data will need to go back into the patient's chart to the start of study timeframe to look at the first seclusion event and use that index seclusion episode (provided the patient met all other eligibility criteria at that time).</i>	Yes	No

Exclusion Criteria

Is the patient prescribed clozapine?	Yes	No
--------------------------------------	-----	----

Appendix 2a

Antipsychotic agents

Short-Acting Antipsychotics	Long-Acting Antipsychotics
Oral Antipsychotics	Aripiprazole LAI
Chlorpromazine	Risperidone LAI
Flupentixol	Paliperidone LAI
Fluphenazine	Haloperidol decanoate
Haloperidol	Fluphenazine decanoate depot IM
Loxapine	Flupentixol decanoate depot IM
Methotrimeprazine	Zuclophenthixol decanoate depot IM
Periciazine	
Perphenazine	
Pimozide	
Thioridazine	
Thiothixene	
Trifluoperazine	
Zuclophenthixol	
Asenapine	
Aripiprazole	
Brexipiprazole	
Cariprazine	
Lurasidone	
Paliperidone	
Olanzapine	
Risperidone	
Quetiapine	
Ziprasidone	
Intramuscular Injectable Antipsychotics	
Haloperidol lactate	
Olanzapine tartrate	
Loxapine	
Zuclophenthixol acetate	

LAI = long-acting injection, IM = intramuscular

Appendix 2b.

Mood stabilizer agents

Drug Name
Lithium
Divalproex
Valproic acid
Lamotrigine
Carbamazepine

Appendix 2c.

Anxiolytic agents

Drug Name
Clonazepam
Lorazepam
Oxazepam
Temazepam
Diazepam
Midazolam
Oxazepam
Nitrazepam
Bromazepam
Alprazolam
Triazolam
Flurazepam
Chlordiazepoxide

Appendix 3.

Lawson Health Research Institute Final Approval Notice



LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-24-112

PROJECT TITLE: The impact of short-acting vs long-acting antipsychotic use on time in seclusion on a forensic assessment unit: a retrospective chart review

PRINCIPAL INVESTIGATOR: Mr Brandon LeBlanc

LAWSON APPROVAL DATE: 4/03/2024 12:00:00 AM

ReDA ID: 14279

Overall Study Status: Active

Please be advised that the above project was reviewed by Lawson Administration and the project was **approved**.

All research must follow applicable laws, regulations, policies, procedures and guidance, including hospital and Lawson policies, and Lawson Standard Operating Procedures.

Please provide your Lawson Approval Number (R# above) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Cory R. Gosnell, B.A. (Hon), MMSc
Interim COO
Lawson Health Research Institute

Tables

Table 1. Baseline characteristics

	Short-acting antipsychotics cohort (n = 60)	Long-acting antipsychotics cohort (n =23)
Median time in seclusion (hours)	66.2 (IQR: 24.4 – 111.2)	37.3 (IQR: 23.2 – 97.7)
Mean age (years)	37.5 (SD ± 12.1)	39.2 (SD ± 12.8)
Male sex at birth	43 (71.7%)	17 (73.9%)
Diagnosis		
Schizophrenia and other related psychotic disorders	54 (90.0%)	22 (95.6%)
Bipolar and related disorders	7 (11.7%)	2 (8.7%)
Mean no. of concomitant antipsychotics*	1.5 (SD ± 1.3)	1.8 (SD ± 1.6)
Mean no. of total antipsychotics prescribed in the last 24 hours of seclusion	1.7 (SD ± 0.7)	2.1 (SD ± 0.9)
Taking mood stabilizer(s)	17 (28.3%)	7 (30.4%)
Taking anxiolytic(s)	47 (78.3%)	21 (91.3%)

IQR = interquartile range, SD = standard deviation

*Any antipsychotic administered after the index antipsychotic during the seclusion period

Table 2. Characteristics of index antipsychotics prescribed

Route of Administration	Short-acting antipsychotics cohort (n = 60)		Long-acting antipsychotics cohort (n =23)	
	Mean daily dose	n	Mean depot dose	n
Intramuscular		19		23
			Aripiprazole 600.0mg	2
	Haloperidol 10.0mg	2	Flupentixol 32.5mg	2
	Loxapine 50.0mg	1	Haloperidol 50.0mg	1
	Olanzapine 10.0mg	3	Paliperidone 127.8mg	11
	Zuclopenthixol 87.5mg	14	Risperidone 50.0mg	1
			Zuclopenthixol 250.0mg	6
Oral		41		N/A
	Haloperidol 9.0mg	5		
	Loxapine 50.0mg	4		
	Olanzapine 12.9mg	12		
	Paliperidone 4.0mg	9		
	Quetiapine 116.7mg	3	N/A	
	Risperidone 2.0mg	6		
	Ziprasidone 40.0mg	1		
	Zuclopenthixol 5.0mg	1		

N/A = not applicable

Table 3. Multivariable regression analysis – primary outcomes

n = 83
R² = 0.05

Variable	Adjusted β (95% CI)	Adjusted p-value
Type of antipsychotic	-2.7 (-67.8 to + 62.4)	0.94
Constant		
Age	-0.73 (-3.1 to + 1.6)	0.54
Gender		
Male	<i>Reference</i>	-
Female	-43.6 (-110.9 to + 23.6)	0.20
Diagnosis		
Bipolar	<i>Reference</i>	-
Schizophrenia	11.3 (-93.8 to +116.4)	0.83

Table 4. Multivariable linear regression – secondary outcomes

			n = 83
			R ² = 0.17
Variable	Adjusted β (95% CI)	Adjusted p-value	
Mood stabilizers			
Long-acting antipsychotics	215.3 (125.5 to 305.1)	p < 0.05	
Short-acting antipsychotics	112.7 (41.2 to 184.2)	p < 0.05	
Anxiolytics			
Long-acting antipsychotics	25.5 (-123.1 to 170.2)	0.74	
Short-acting antipsychotics	25.3 (-52.9 to 103.4)	0.52	

Figures

Figure 1. Study Enrollment

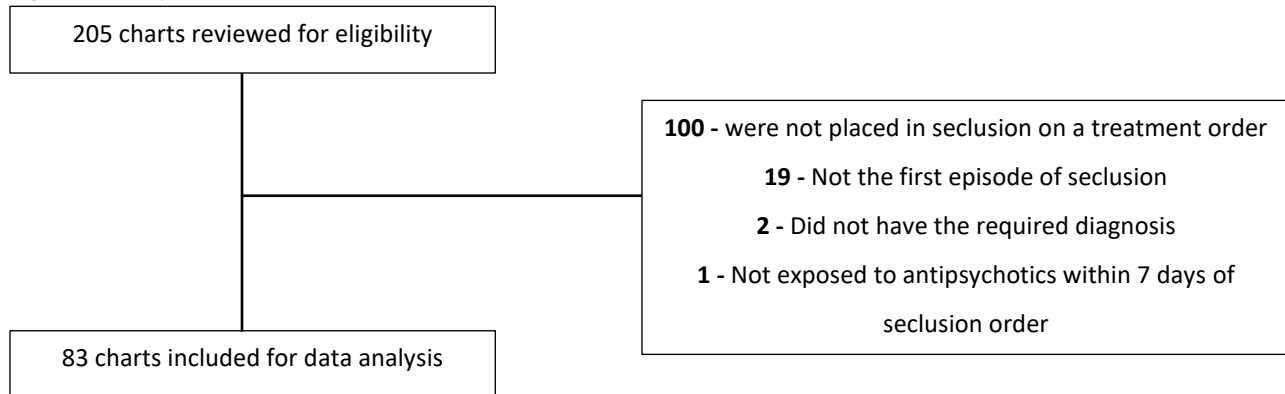


Figure 2. Box and whisker plot for time in seclusion for LA and SA antipsychotic cohorts

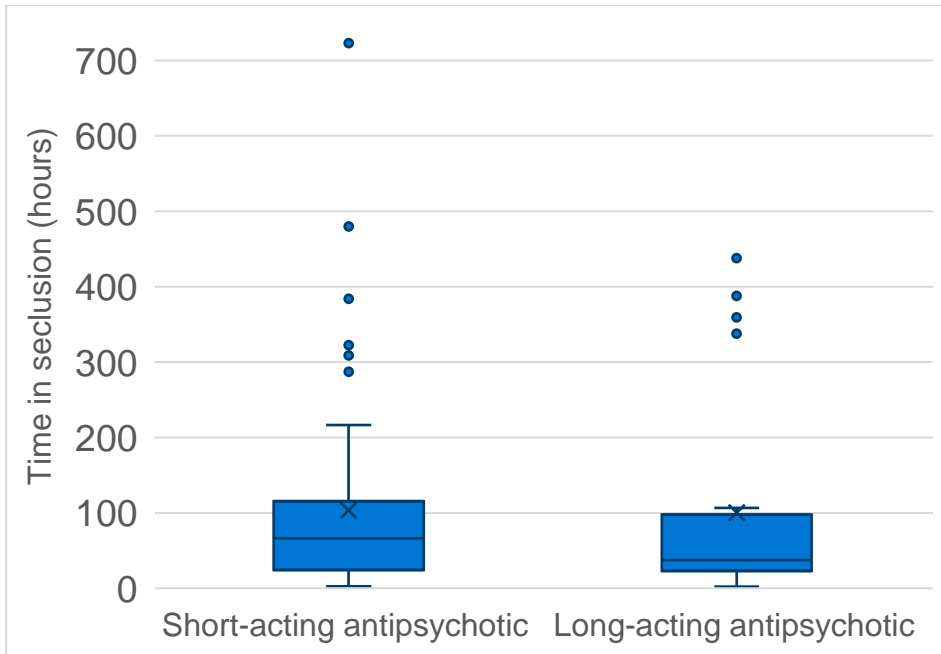


Figure 3. Antipsychotic administration in last 24 hours of seclusion

